Citation:

Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH, Manson JE. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr.* 2000 Jun;71(6):1455-61.

PubMed ID: 10837285

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine prospectively:

- Whether dietary glycemic load is related to risk of CHD
- Whether the glycemic index can predict risk of CHD better than can the traditional classification of carbohydrates into simple and complex forms
- Whether the relation of glycemic load to risk of CHD is modified by adiposity

Inclusion Criteria:

- Women aged 38 - 63 years with no previous diagnosis of diabetes mellitus, myocardial infarction, angina, stroke or other cardiovascular diseases at baseline in 1984
- Women returning the semiquantitative food frequency questionnaire and had daily intakes between 600 - 3500 kcal

Exclusion Criteria:

- Women with previously diagnosed diabetes (n = 2248) and cardiovascular disease (including angina, myocardial infarction, stroke and other cardiovascular diseases, n = 3122)

Description of Study Protocol:

Recruitment

- The Nurses' Health Study was initiated in 1976 when 121,700 female registered nurses aged 30 - 55 years answered a mailed questionnaire about their medical histories and lifestyles
- Dietary information collected in 1984
- The cohort has been followed up every 2 years to ascertain exposure and incident diseases

Design: Prospective cohort study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

- For each participant, person-years of follow-up were counted from the date of return of the 1984 questionnaire to the date of CHD diagnosis, the date of death, or 1 June 1994, whichever came first
- Women were grouped in quintiles of glycemic load, overall dietary glycemic index, and carbohydrate intake (simple or complex).
- Incidence rates were calculated as the number of CHD events divided by the person-time of follow-up in each quintile
- Incidence rate ratios were calculated by dividing the incidence rate of CHD in a particular category of exposure by the corresponding rate in the reference category
- Tests for trends were conducted by assigning the median value to each quintile and modeling this value as a continuous variable
- The log likelihood ratio test was used to assess the significance of the interaction terms
- In multivariate analyses, the estimated relative risks were simultaneously adjusted for potential confounding variables by using a pooled logistic regression that was asymptotically equivalent to the Cox proportional hazards regression

Data Collection Summary:

Timing of Measurements

- Women were followed for 10 years (1984 - 1994)
- All dietary variables were updated in 1986 and 1990

Dependent Variables

- Risk of coronary heart disease
- Incident CHD, including fatal CHD and nonfatal MI, confirmed by medical records, autopsy reports, death certificates or the National Death Index

Independent Variables

- Dietary glycemic load and carbohydrate intake
- Each participant's dietary glycemic load was calculated as a function of glycemic index, carbohydrate content, and frequency of intake of individual foods reported on a validated food frequency questionnaire at baseline

Control Variables

- Age
- BMI
- Smoking status
- Alcohol intake
- Physical activity
- Postmenopausal hormone use

- Multivitamin use
- Use of vitamin E supplements
- Parental history of myocardial infarction before age 60 years
- History of hypertension
- History of hypercholesterolemia
- Total energy intake

Description of Actual Data Sample:

Initial N: 121,700 female nurses at baseline in 1976, 81,757 returned the food frequency questionnaire

Attrition (final N): 75,521 female nurses included in the analysis

Age: aged 30 - 55 years in 1976, aged 38 - 63 years in 1984

Ethnicity: predominantly white

Other relevant demographics:

Anthropometrics

Location: United States

Summary of Results:

Key Findings

- At baseline in 1984, the mean dietary glycemic load varied nearly 2-fold between the highest and lowest quintiles of the study population
- During 10 years of follow-up (729,472 person-years), 761 cases of CHD (208 fatal and 553 nonfatal) were documented
- Dietary glycemic load was directly associated with risk of CHD after adjustment for age, smoking status, total energy intake and other coronary disease risk factors
- The relative risks from the lowest to highest quintiles of glycemic load were 1.00, 1.01, 1.25, 1.51 and 1.98 (95% confidence interval: 1.41 to 2.77 for the highest quintile, P for trend < 0.0001).
- Carbohydrate classified by glycemic index, as opposed to its traditional classification as either simple or complex, was a better predictor of CHD risk
- The association between dietary glycemic load and CHD risk was most evident among women with body weights above average (BMI > 23).

Adjusted Relative Risks (95% CIs) of CHD According to Quintiles of Energy-Adjusted Glycemic Load among 75,521 US Female Nurses Aged 38 - 63 years, 1984 - 1994

	Quintile 1 (lowest)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (highest)
Cases of CHD	139	128	148	160	186
Person-years	147,341	141,515	146,413	149,977	144,226

Relative risk (95% CI) for Model 1 (adjusted for age and smoking)	1.00	0.92 (0.73, 1.17)	1.08 (0.85, 1.36)	1.27 (1.01, 1.59)	1.57 (1.27, 1.95)
Relative risk (95% CI) for Model 2 (multivariate, without fats)	1.00	0.94 (0.73, 1.20)	1.11 (0.86, 1.43)	1.28 (0.98, 1.66)	1.56 (1.17, 2.07)
Relative risk (95% CI) for Model 3 (multivariate, with additional adjustment for saturated and *trans* fats)	1.00	0.97 (0.76, 1.25)	1.19 (0.92, 1.55)	1.42 (1.07, 1.88)	1.85 (1.34, 2.54)
Relative risk (95% CI) for Model 4 (multivariate, with additional adjustment for all fats)	1.00	1.01 (0.78, 1.64)	1.25 (0.96, 1.64)	1.51 (1.13, 2.03)	1.98 (1.41, 2.77)

Author Conclusion:

These findings suggest that a high intake of rapidly digested and absorbed carbohydrate increases the risk of CHD independent of conventional coronary disease risk factors. These data add to the concern that the current low-fat, high-carbohydrate diet recommended in the United States may not be optimal for the prevention of CHD and could actually increase the risk in individuals with high degrees of insulin resistance and glucose intolerance.

Reviewer Comments:

10 year follow-up. Multiple measurements of dietary intake.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes